REMARKS

Reconsideration of this patent application is respectfully requested in view of the foregoing amendments, and the following remarks.

The amendments to this patent application are as follows. The Specification has been amended to update the status of the Parent U.S. Patent Application. Also claims 47,50,53,61 to 62, 65 to 66 and 68 have been amended to overcome the formal objections against these claims. Claims 48,49,51,52 and 54-60 and 69 have been cancelled; and new claim 73 has been added.

Reconsideration and withdrawal are respectfully requested for the double patenting rejection.

The present application is a Divisional of U.S. Patent No. 6,423,516. The Patent Examiner stated that pending claims 47-68 and 70-72 are unpatentable over claims 1, 3-5 and 13 of the aforementioned US patent because the method of claims 1, 3-5 and 13 of US Patent No. 6,423,516 is allegedly a genus that would be obvious in view of the species of method claims 47-72 of the instant application.

The main claim of the U.S. Patent No. 6,423,516 is drawn to a method of destabilizing viral quasi-species comprising

treating a target cell with a replicator nucleic acid.

In contrast to the above mentioned U.S. Patent No. 6,423,516 the present invention is drawn to a process for destabilizing a viral quasi-species distribution by means of a defective replication system, whereby the agent to reach this result is further specified in former claim 49, now incorporated by claim 47. Pending claim 47 is drawn to a process wherein the defective replication system is induced by action of a chemical substance active agent. Therefore, the Divisional Patent Application focuses on chemical substances to destabilize the viral quasi-species-distribution. It was the intention of the Divisional Patent Application to bring out the chemical substance approach in general.

Therefore, the process is not limited to the negative interference of the replication of the consensus sequence (nucleic acid sequence of the viral wild-type) by a replicator nucleic acid as described in the U.S. Patent No. 6,423,516. The process of the present invention and the Divisional Patent Application affects the misincorporation of nucleotides by means of chemical substances.

Moreover, it is the understanding of the applicant that the method of the present application fulfills all

requirements of 35 U.S.C. 121 (divisional applications). Hence the double patenting rejection is not applicable and should be withdrawn.

To emphasize the chemical substance approach of the present invention, another dependent claim is now being added that is directed to the identification of such a chemical substance. This new claim 73 is based on the Specification on page 6, right column, paragraph [0066] (ref. according to U.S. Patent Application Publication 2002/107220 A1) and includes the following steps:

A process for identification of a chemical substance (active agent) according to claim 49 comprising

(a) incubation of the replication system of cloned variants of the wild-type virus in infected target cells with purative active agents of different concentrations, and

(b) detection of incorrect virus variants and therefore identification of the active agent.

Thus, a procedure for utilizing the chemical substance is emphasized. Claims 48,49,51,52 and 54 to 60, that are mainly drawn to the provision of a defective replication system by infiltration of the same into the virus population, have been cancelled.

The typographical errors in claims 65 ("eucaryocic" instead of "eukaryotic") and 68 ("metagenesis" instead of "mutagenesis" and "quadi-species" instead of "quasi-species") have been corrected.

Regarding the Examiner's objections, under 35 U.S.C. 112 to certain claims, the following amendments are being incorporated into the claims:

a) Claim 50 is being amended by adding the word "comprising" in front of the phrase "selecting". The Examiner proposed to add "further comprising" before the phrase "selecting" but the word "further" indicates "additional" and maybe alternative step in the process whereby the process step of claim 50 is connected to the process steps as disclosed by the previous claim. The step selecting a chemical substance from the group consisting of an antimetabolite and an allosteric effector is connected to inducing the defective replication of the viral nucleic acid by action of this chemical substance (claim 47). These two steps could not be considered separate.

b) Claim 61 is being amended by adding the phrases "the treatment of viral infections" and "in a patient" in the preamble of the claim. The Examiner objects to the accomplishing step of the process by treating a human being.

To clarify the process of treatment or prophylaxis the added term "in a patient" is based on the specification page 3, left column, fourth paragraph (according to the publication), where the undesired resistance phenomena that occurs during treatment of infected patients are described. These phenomena can be prevented by the process of treatment or prophylaxis of viral diseases in a patient. According to claim 47 the part regarding the infiltration of a viral system has been deleted.

c) Claim 62 is being amended by changing the dependency to amended claim 61 and deleting the phrase "host cells are" and the word "and" after the word "infection" and adding the phrase "or viral disease". The Examiner objects to the phrase "host cells are the target cells of the viral infection.." as being vague and indefinite. The applicant agrees that the term "host cells" has no antecedent basis in claim 47 but referring to the specification (page 5, left column, fourth paragraph) target cells and host cells are meant to be the same. Therefore, the term "host cells" can be deleted. The term "or viral disease" is added to point out the dependency to amended claim 61 wherein the treatment of viral infections on one hand and the treatment of viral diseases in a patient on the other hand is disclosed.

d) Claim 66 is being amended by replacing the phrase "wherein they are" with "comprising". The Examiner states that the word "they" is vague and indefinite because it is not clear what "they" encompasses in claim 63.

For all these reasons, the Specification and all the claims are in complete compliance with the requirements of 35 U.S.C. 112. Withdrawal of this ground of rejection is respectfully requested.

Claims 63-66 have been rejected under 35 U.S.C. 102 as anticipated by *Ikeda et al.* (EP 0 215 987 A1). *Ikeda et al.* discloses a reverse transcriptase encoded by cauliflower mosaic virus, a gene encoding the transcriptase, a recombinant DNA containing the cloned gene and living cells involving the recombinant DNA.

It is argued that *Ikeda et al.* discloses an agent comprising a nucleic acid and a polypeptide encoded by the nucleic acid that is able to destabilize the viral quasi-species-distribution. But as discussed before, the present invention is not limited to such agents named by *Ikeda et al.* to destabilize the viral quasi-species-distribution but moreover to chemical substance to induce a defective replication to the virus population without stimulating the formation of resistant virus populations. It is an object of

the present divisional application to focus on this chemical substance approach in general. Therefore, a discussion of the claims 63 to 66 is based on the information disclosed in the specification. The most relevant passages of the specification providing information on the agent are as follows (ref. according to U.S. Patent Application Publication 2002/0107220 A1, accentuation added on this side):

a) page 2, paragraph [0010]: The object of the invention is to provide a generally applicable process by which the virus population lose certain pathogenic properties, particularly the property of infectiousness. Related to this is the provision of an agent by which viral infections can be treated therapeutically and prophylactically without stimulating the formation of resistent virus populations. [...].

b) page 3, paragraph [0029]: The defective replication of the viral nucleic acid can be induced, according to the invention, preferably by action of a chemical substance. In this case, the substance can act as an antimetabolite or allosteric effector of the replication system. The substance is preferably of such a kind that it does not interact with the cellular enzyme system, in order to prevent, optionally,

the toxic side effects. [...]

c) page 6, paragraph [0065]:[...] In this way, an active agent which interferes with the replication process in a way that it comes to a specific elevation of the rate of misincorporation of the viral replication system, can be used. [...]

d) page 6, paragraph [0066]: The screening to HIV is carried out, e.g., with cloned HIV variants in infected target cells[...]. Thereby, the virus replicating system is incubated with potential active agents of different concentrations. A representative gene locus of the virus RNA or virus DNA is then [...] examined by a detection system as described in PCT/EP 90/01366 for the presence of incorrect virus variants which are amplified within the cells. In this way, such active agents can be detected that exceed the error threshold, which, however, do not prevent a replication and not necessarily influence measurably the infectivity. [...]

Thus, the Specification of the present invention provides a sufficient disclosure of a broad range of chemical substances or agents to carry out the inventive process and also to a process to identify the same. Thus the prior art reference fails to teach or to suggest this claimed subject matter.

In summary, claims 47,50,53,61,62,65 to 66 and 68 have been amended. Claims 48,49,51,52,54 to 60 and 69 have been cancelled. New claim 73 has been added.

There can be no double patenting rejection because of a Restriction Requirement under 35 U.S.C. 121. The above amendments to the claims overcome all of the formal grounds of rejection under 35 U.S.C. 112. In addition, all of the claims are not anticipated under 35 U.S.C. 102, but are patentable under 35 U.S.C. 103, in view of the prior art of record. A prompt notification of allowability is respectfully requested.

Respectfully submitted,

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Enclosures: 1) Copy of Petition 3 Month Extension of Time Large Entity

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to: Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on February 26, 2004.

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Maria Guastella